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DAVIDSON, DAVIDSON & KAPPEL, LLC 485 SEVENTH AVENUE, 14TH FLOOR NEW YORK, NY 10018			EXAMINER SASAN, ARADHANA	
			ART UNIT 1615	PAPER NUMBER
			MAIL DATE 12/12/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/817,335

Applicant(s)

STANIFORTH ET AL.

Examiner

Aradhana Sasan

Art Unit

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 September 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4,5,7-12 and 39-52 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,5,7-12 and 39-52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>4/2/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 09/14/2007 are acknowledged.
2. Claim 39 was amended.
3. Claims 1, 2, 4, 5, 7-12, 39-52 are included in the prosecution.

Response to Arguments

Information Disclosure Statement

4. Applicant's submission of the reference "Machines Collette High Shear Mixer Granulator Promotional Literature" is acknowledged. See attached copy of PTO-1449.

Specification

5. Applicant's amendment to the specification to include cross reference to the related application is acknowledged.

Objection to claim 39

6. In light of applicant's amendment of claim 39, the claim objection is withdrawn.

Obviousness-type Double Patenting Rejection

7. Applicant did not point out that the obviousness-type double patenting rejection was improper. This is considered non-responsive. Applicant must point out the reasons why the obviousness-type double patenting rejection is improper or file a terminal disclaimer in order to be responsive. Until such time that a terminal disclaimer is filed, the obviousness-type double patenting rejection will be maintained.

Rejection of claims 1, 2, 4, 5, 7-12, and 39-52 under 35 USC § 103(a)

8. Applicant's arguments, see Page 9, filed 09/14/2007, with respect to the rejection of claims 1, 2, 4, 5, 7-12, and 39-52 under 35 USC § 103(a) as being unpatentable over Schmidt et al. (US 4,605,666) have been fully considered but are not persuasive.

Applicant argues that the Schmidt reference does not teach or suggest "forming an aqueous slurry containing a mixture of microcrystalline cellulose in the form of wet cake and silicon dioxide ...; drying said slurry to obtain an excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with said silicon dioxide as recited in independent claim 1". Applicant argues that the Schmidt reference does not teach or suggest "(a) forming an aqueous slurry of microcrystalline cellulose in the form of wet cake; (b) forming an aqueous slurry of silicon dioxide having a particle size of from about 1 nm to about 100 μ m; (c) separately introducing said microcrystalline cellulose slurry and said silicon dioxide slurry separately into a drying apparatus for combination therein, to obtain an excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with said silicon dioxide as recited in independent claim 39 of the present invention" (Page 11).

This is not persuasive because Schmidt teaches an aqueous slurry of ascorbic acid, microcrystalline cellulose and water, which is spray dried and then silicon dioxide is added (Col. 3, lines 29-49). Silicon dioxide is disclosed as the adsorbent (Col. 7, lines 14-15). A person having ordinary skill in the art at the time the invention was made could have used the aqueous slurry taught by Schmidt and included the adsorbent

Art Unit: 1615

silicon dioxide into the slurry prior to spray drying instead of adding it to the spray dried mixture. This would have been part of the routine experimentation strategy to optimize the compressibility of the final tablet. Moreover, a "plurality of agglomerated particles" is essentially a mixture. Prior to tableting, the excipients and active ingredient are mixed; therefore a "plurality of agglomerated particles" would be achieved.

Applicant argues that the examiner is relying on impermissible hindsight by stating that a person having ordinary skill in the art at the time the invention was made could have used the aqueous slurry taught by Schmidt and that there is no basis provided in the Schmidt reference for one of skill in the art to utilize the silicon dioxide as an adsorbent that is separately added within the drying chamber at a point of negative pressure (Page 11).

This is not persuasive because it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant argues that a person having ordinary skill in the art "would still not arrive at the present invention which requires the formation of a "pre-manufactured" excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with the silicon dioxide, prior to the addition of an active agent, which mixture is then compressed into a tablet". Applicant states that "instead they

Art Unit: 1615

would obtain a mixture of the active agent, microcrystalline cellulose and silicon dioxide” (Page 12).

This is not persuasive because a person skilled in the art would have used the aqueous slurry taught by Schmidt and included the adsorbent silicon dioxide into the slurry prior to spray drying instead of adding it to the spray dried mixture during the process of routine experimentation and arrived at a plurality of agglomerated particles of microcrystalline cellulose in intimate association with silicon dioxide which is the “pre-manufactured excipient” comprising microcrystalline cellulose and silicon dioxide.

Therefore, the rejection of 3/6/07 is maintained.

MAINTAINED REJECTIONS:

The following is a list of maintained rejections:

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1, 2, 4-5, 7-12, and 51-52 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 20, 21, 23-27 of U.S. Patent No. 6,103,219. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1, 2, 4-5, 7-12, and 51-52 are drawn to a method for preparing a tablet comprising: forming an aqueous slurry containing a mixture of microcrystalline cellulose in the form of a wet cake and silicon dioxide having a particle size from about 1 nm to about 100 μm ; drying said slurry to obtain an excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with said silicon dioxide, the amount of silicon dioxide being from about 0.1% to about 20% relative to the amount of microcrystalline cellulose, by weight; mixing an active ingredient with said excipient in a ratio from about 1:99 to about 99:1 to obtain a mixture; compressing said mixture into a tablet.

Claims 20, 21, 23-27 of U.S. Patent No. 6,103,219 ('219) are drawn to a method of preparing a solid dosage form comprising steps identical to those listed above from the instant application. One skilled in the art would recognize that the method of preparing a solid dosage form taught in '219, also includes tablets. The claimed subject matter of the instant application is taught by '219. Forming an aqueous slurry containing a mixture of microcrystalline cellulose in the form of a wet cake and silicon dioxide

Art Unit: 1615

having a particle size from about 1 nm to about 100 μm ; drying said slurry to obtain an excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with said silicon dioxide, the amount of silicon dioxide being from about 0.1% to about 20% relative to the amount of microcrystalline cellulose, by weight; mixing an active ingredient with said excipient in a ratio from about 1:99 to about 99:1 to obtain a mixture; and incorporating said mixture into a plurality of solid unit doses.

Claim 2 of the instant application is anticipated by claim 21 of '219.

Claim 4 of the instant application is anticipated by claim 24 of '219.

Claim 5 of the instant application is anticipated by claim 25 of '219.

Claim 7 of the instant application is anticipated by claim 27 of '219.

Claims 8-12 of the instant application are drawn to a method of further drying the aqueous slurry so the moisture content of the excipient particles can be controlled. Since the technique of spray drying is used and it is well known in the art, varying the parameters of the spray drying procedure could modify the moisture content of the excipient particles.

Claim 51 of the instant application is anticipated by claim 23 of '219.

Claim 52 of the instant application is anticipated by claim 26 of '219.

Therefore, the claimed subject matter, i.e. a method for preparing a tablet by mixing an active ingredient with the excipient (prepared after forming a slurry containing a mixture microcrystalline cellulose and silicon dioxide, and drying the slurry to get agglomerated particles of microcrystalline cellulose in intimate association with silicon dioxide) and compressing the mixture into a tablet, are anticipated by '219.

Art Unit: 1615

11. Claims 39-42, and 46-50 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 19, 20, 24, 30, 32, and 33 of U.S. Patent No. 6,746,693 in view of claims 25-27 of U.S. Patent No. 6,103,219.

Although the conflicting claims are not identical, they are not patentably distinct from each other.

Instant claims are drawn to a method for preparing a tablet, comprising the steps of: (a) forming an aqueous slurry of microcrystalline cellulose in the form of wet cake; (b) forming an aqueous slurry of silicon dioxide having a particle size of from about 1 to about 100 μ m; (c) separately introducing said microcrystalline slurry and said silicon dioxide slurry separately into a drying apparatus for combination therein, to obtain an excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with said silicon dioxide, the amount of silicon dioxide being from about 0.1% to about 20% relative to the amount of microcrystalline cellulose, by weight; (d) mixing an active ingredient with said excipient in a ratio of from about 1:99 to about 99:1 to obtain a mixture; (e) compressing said mixture into a tablet.

Claims 19, 20, 24, 30, 32, and 33 of U.S. Patent No. 6,746,693 ('693) are drawn to a method of preparing a solid dosage form comprising steps identical to those listed above from the instant application. One skilled in the art would recognize that the method of preparing a solid dosage form taught in '693, also includes tablets. The claimed subject matter of the instant application is taught by '693. Forming separate aqueous slurries of microcrystalline cellulose and silicon dioxide and introducing these slurries separately into a drying apparatus to obtain an excipient comprising a plurality

Art Unit: 1615

of agglomerated particles of microcrystalline cellulose in intimate association with the silicon dioxide, the amount of silicon dioxide being from about 0.1% to about 20% relative to the amount of microcrystalline cellulose, mixing an active ingredient with the agglomerated particles, and incorporating the mixture into a plurality of solid unit doses.

Claim 39 of the instant application includes a ratio of active ingredient and excipient of 1:99 to about 99:1. Claim 19 of '693 does not teach this ratio. However, in US 6,103,219 ('219), claim 20 teaches mixing an active ingredient with an excipient in a ratio from about 1:99 to about 99:1. It would have been obvious to one having ordinary skill in the art at the time the invention was made to combine the teaching of '693 (which includes using separate slurries of microcrystalline cellulose and silicon dioxide) with the ratio of active ingredient to excipient taught by '219.

Claim 40 of the instant application is anticipated by claims 20 (further comprises wet granulating the mixture before incorporating into solid unit doses) and 24 (colloidal silicon dioxide) of '693.

Claim 41 of the instant application is anticipated by claim 30 (particle size from 10 μ m to 1000 μ m) and claim 37 (spray drying) of '693.

Claim 42 of the instant application is anticipated by claim 32 of '693.

Claims 46-50 of the instant application are anticipated by claim 33 of '693 (which teaches that the moisture content of the particles is from 0.5-15%). Claims 47, 48, 49, and 50 are covered by the range 0.5-15% of the moisture content.

Therefore, the claimed subject matter, i.e. a method for preparing a tablet by mixing an active ingredient with the excipient (prepared after forming separate slurries

of microcrystalline cellulose and silicon dioxide and drying the slurry to get agglomerated particles of microcrystalline cellulose in intimate association with silicon dioxide) and compressing the mixture into a tablet, are anticipated by '693.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claims 1, 2, 4, 5, 7-12, and 39-52 rejected under 35 U.S.C. 103(a) as being unpatentable over Schmidt et al. (US 4,605,666).

Claims 1, 2, 4, 5, 7-12, and 39-52 are drawn to a method for preparing a tablet comprising: forming an aqueous slurry containing a mixture of microcrystalline cellulose in the form of a wet cake and silicon dioxide having a particle size from about 1 nm to about 100 μ m; drying said slurry to obtain an excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with said silicon dioxide, the amount of silicon dioxide being from about 0.1% to about 20% relative to the amount of microcrystalline cellulose, by weight; mixing an active ingredient with said excipient in a ratio from about 1:99 to about 99:1 to obtain a mixture; compressing said mixture into a tablet.

Schmidt teaches a "process for preparing a powder ... which is directly compressible into a tablet prepared by spray drying (a) an aqueous slurry of a water-soluble vitamin and a binder; (b) ... an adsorbent; and (c) a lubricant" (Abstract). It is

Art Unit: 1615

taught that “the powders are directly compressible into tablets and will not demix” (Abstract). In example 1 an aqueous slurry of ascorbic acid, microcrystalline cellulose and water is spray dried and silicon dioxide is added (Col. 3, lines 29-49). The adsorbent is silicon dioxide (Col. 7, lines 14-15) and the binder is microcrystalline cellulose (Col. 8, lines 4-5).

A person having ordinary skill in the art at the time the invention was made could have used the aqueous slurry taught by Schmidt and included the adsorbent silicon dioxide into the slurry prior to spray drying instead of adding it to the spray dried mixture. This would have been part of the routine experimentation strategy to optimize the compressibility of the final tablet. The microcrystalline cellulose in wet cake of the instant claims is known in the art as hydrocellulose and would be readily available. The silicon dioxide used in tableting is known in the art and using the 1nm to about 100 μ m silicon dioxide would be a parameter that the experimenter would find obvious. A “plurality of agglomerated particles” is essentially a mixture. Prior to tableting, the excipients and active ingredient are mixed; therefore a “plurality of agglomerated particles” would be achieved. The percentage of silicon dioxide (“from about 0.1% to about 20%”) would be obvious to one skilled in the art as a variable that could be adjusted to achieve the desired flow rate and compressibility. Similarly, the ratio of active ingredient to the excipient would be obvious to one skilled in the art as an adjustable variable to achieve the desired release rate, stability, etc.

Regarding instant claim 39, a person having ordinary skill in the art could use the teaching of Schmidt and prepare separate aqueous slurries of microcrystalline cellulose

Art Unit: 1615

and silicon dioxide prior to spray drying as part of routine experimentation in order to determine which resultant excipient offered the best compressibility.

Instant claim 2, which discloses colloidal silicon dioxide and wet granulating the mixture before compressing into tablets, would have been obvious to one skilled in the art of tableting. The use of colloidal silicon dioxide is a well-known practice, as is wet granulation of a "premix" before tableting.

By modifying the teaching of Schmidt regarding spray drying the aqueous slurry to include an aqueous slurry of microcrystalline cellulose and silicon dioxide, and manipulating the spray drying process parameters, an experimenter would achieve the excipient particle size range (disclosed in instant claims 4, 41, 42, and 51) and the bulk density range (disclosed in instant claims 5, 43, 44, and 52). Also, an obvious variation of experimentation would include adding extra excipient to the mixture before tableting (instant claims 7 and 45) in order to improve flowability and compressibility.

Regarding instant claims 8-12 and 46-50, a person having ordinary skill in the art could modify the teaching of Schmidt and further adjust the spray drying process parameters to achieve the moisture content ranges disclosed.

Therefore, it would have been obvious to a person having ordinary skill in the art at the time the invention was made to prepare a tablet using the teaching of Schmidt and modifying the parameters during routine experimentation and arrive at the claimed invention.

Conclusion

14. No claims are allowed.

Art Unit: 1615

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.


16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

Art Unit: 1615

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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